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| EXAMINER | |
|---|---|
| LU, FRANK WEI MIN | |
| **ART UNIT** | **PAPER NUMBER** |
| 1634 | |

DATE MAILED: 04/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

SM.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/814,252 | HANSON ET AL. | |
| | Examiner | Art Unit | |
| | Frank W Lu | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 March 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *11,17,38,56 and 57* is/are pending in the application.

4a) Of the above claim(s) *17 and 38* is/are withdrawn from consideration.

5)☒ Claim(s) *11* is/are allowed.

6)☒ Claim(s) *56 and 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

## CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission of RCE filed on March 2, 2004 and the amendment filed on January 27, 2004 have been entered. The claims pending in this application are claims 11, 17, 38, 56, and 57. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of amendment filed on January 27, 2004.

**2. Response to Arguments of Restriction Requirement**

In page 5, third paragraph of applicant's remarks, applicant argues that "[A]lthough Applicants do not agree with the Restriction Requirement, all claims to primers, methods or kits that do not include reference to the PSE1, PSE4, CARB3 beta-lactamase enzymes have been canceled. Applicants have also amended method claims 17 and 38 to be specific to such enzymes. Thus, reconsideration and withdrawal of the restriction with respect to these two method claims is respectfully requested. Because the kit claims with analogous language have been examined, it is respectfully submitted that this should not involve an undue burden.".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the restriction requirement. First, the restriction was made final in the office action mailed on April 8, 2003. Second, applicant has amended claim 17 in the amendment filed

on January 27, 2004. For example, a phrase "each having 15-35 nucleotides, specific for nucleic acid characteristic PSE1, PSE4, and CARB3 beta-lactamase enzymes" has been added into claim 17. Since the examiner only examined claims 11, 56, and 57 in previous office actions, which are directed to a primer and a kit comprising said primer, amended claims 17 and 38, which is directed to a method for identifying a PSE1, PSE4 or CARB3 family beta-lactamase, is directed to an invention that is independent or distinct from the invention originally claimed . Since applicant has received an action on the merits for the originally presented invention, this invention (claims 11, 56, and 57) has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 17 and 38 withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Third, although the searches for amended method claims 17 and 38 and kit claims 56 and 57 may have some overlap, the searches for amended method (claims 17 and 38) and kit (claims 56 and 57) are not coextensive. For example, a search for "separating and analyzing" step of claim 17 is not required for kit claims 56 and 57. Therefore, claims 11, 56, and 57 will be examined.

***Claim Objections***

3. Claim 56 is objected to because of the following informality: "Gram Negative organisms" should be "Gram Native bacteria".

Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 56 and 57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is referred to the interim guidelines on written description published on December 21, 1999 in the Federal Register at Volume 64, Number 244, pp.71427-71440.

*Vas-Cath Inc. v. Mahurkar,* 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116.

The specification provides adequate written descriptions for Gram Negative bacteria (for example, see page 4, second paragraph). However, the specification fails to adequately describe any kind of Gram Negative organism. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention

in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998).

In this instant case, although the specification adequately describes Gram Negative bacteria, the specification fails to adequately describe any kind of Gram Negative organism. Furthermore, it is unclear, besides Gram Negative bacteria, whether there is another organism that can be called as a Gram Negative organism. Therefore, the general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed.

With limited disclosure provided by the specification, the skilled artisan cannot envision all claimed Gram Negative organisms and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method used. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co.* Ltd., 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what e has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

## *Claim Rejections - 35 USC § 103*

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claim 56 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sandvang *et al.*, (FEMS Microbiology Letters, 157, 177-181, December 1997) in view of Fluit *et al.*, (WO91/08305, published on June 13, 1991).

The claimed inventions are drawn to a diagnostic kit. Claim 56 requires that a diagnostic kit for detecting a PSE1, PSF4, or CARB3 family beta-lactamase comprising: (a) at least one primer pair capable of hybridizing to a beta-lactamase nucleic acid characteristic of the PSE1, PSE4, and CARB3 family of beta-lactamase enzymes wherein each primer of the pair includes 15-35 nucleotides; (b) a positive and negative control; and (c) a protocol for identification of the beta-lactamase nucleic acid of interest.

Sandvang *et al.,* teach characterization of integrons and antibiotic resistance genes in Danish multiresistant *Salmonella enterica* Typhimurium DT104. They used two PSE-1 primers, pse-1 F (nucleotides 323 to 342 in forward sequence, 20 bp) and pse-1 B selected from PSE-1 beta-lactamase gene (nucleotides 742 to 723 in reverse sequence, 20bp), to amplify an integron containing PSE-1 beta-lactamase gene (see abstract in page 177 and primer numbers 9 and 10 of Table 2 in page 179).

Regarding claim 56, since two PSE-1 primers, pse-1 F and pse-1 B, are 20 bp and used to amplify a PSE-1 beta-lactamase gene in the method taught by Sandvang *et al.*,(see Table 2 in page 179), pse-1 F and pse-1 B are a primer pair capable of hybridizing to a beta-lactamase nucleic acid characteristic of the PSE1, PSE4, and CARB3 family of beta-lactamase enzymes wherein each primer of the pair includes 15-35 nucleotides as recited in (a) of the claim because these primers hybridize with PSE-1 beta-lactamase gene during the process of amplifying an integron containing PSE-1 beta-lactamase gene. Since strain *Salmonella enterica* Typhimurium DT104 with designation 9412445 is antibiotic sensitive while strain *Salmonella enterica* Typhimurium DT104 with designation 9616368 is antibiotic resistance on Ap, Cm, Sp, Sm, Su, and Te (see table 1 in page 178), strain *Salmonella enterica* Typhimurium DT104 with designation 9412445 and strain *Salmonella enterica* Typhimurium DT104 with designation 9616368 are positive and negative controls respectively for *Salmonella enterica* Typhimurium DT104 with designation 9423245 which is antibiotic resistance on Sp, Sm, and Su as recited in (b) of the claim. Since the method taught by Sandvang *et al.,* includes to identify the integron containing pse-1 beta-lactamase gene from bacterial strains, *Salmonella enterica* Typhimurium DT104, using PCR and sequencing (see abstract in page 177), the method taught by Sandvang *et*

*al.,* is a protocol for identification of the beta-lactamase nucleic acid characteristic of the PSE1, PSE4, and CARB3 family of beta-lactamase enzymes as recited in (c) of the claim.

Sandvang *et al.,* do not disclose a bacteria diagnostic kit as recited in claim 56.

Fluit *et al.,* do teach a bacteria diagnostic kit (see pages 24 and 25).

Therefore, it would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to have organized the components and method taught by Sandvang *et al.,* into a kit because the method for identifying a beta-lactamase in a bacteria sample using PCR and sequencing is known at that time the inventions were made and the kit format is utilized not only to assemble a variety of different reagents together but ensure the quality and compatibility of the reagents. One having ordinary skill in the art at the time the invention was made would have been motivated to assemble reagent (s) of biotechnology methods into a kit in order to obtain the above discussed advantages, thus resulting in instant kit recited in claim 56. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to combine these prior art together because the kit would provide a convenient, efficient, economical way to practice the method of Sandvang *et al.*.

8. Claim 56 is rejected under 35 U.S.C. 103(a) as being unpatentable over Arlet *et al.,* (FEMS Microbiology Letter, 82, 19-26, 1991) in view of Fluit *et al.,* (WO91/08305, published on June 13, 1991).

The claimed inventions are drawn to a diagnostic kit. Claim 56 requires that a diagnostic kit for detecting a PSE1, PSF4 or CARB3 family beta-lactamase comprising: (a) at least one

primer pair capable of hybridizing to a beta-lactamase nucleic acid characteristic of the PSE1, PSE4, and CARB3 family of beta-lactamase enzymes wherein each primer of the pair includes 15-35 nucleotides; (b) a positive and negative control; and (c) a protocol for identification of the beta-lactamase nucleic acid characteristic of the PSE1, PSE4, or CARB3 family of beta-lactamase enzymes.

Arlet *et al.*, teach construction by polymerase chain reaction and intragenic DNA probes for three main types of transferable beta-lactamases (TEM, SHV, CARB). A CARB probe was amplified in the presence of primers OC-1 (nucleotides 335-354 for forward sequence, 20 bp) and OC-2 (nucleotides 909-922 for reverse sequence, 20 bp) selected from PSE-4 gene (see Table 2 in page 21 and left column in page 22, and reference 10 cited by this paper). The CARB probe hybridized with PSE-1, PSE-4, CARB-2, and CARB-3 and CARB-4 (see page 23, right column).

Regarding claim 56, since two SHV primers OC-1 and OC-2 are 20 bp and are used to amplify a CARB beta-lactamase gene probe in the method taught by Arlet *et al.*,(see Table 2 in page 21, left column in page 22, and Figure 1 in page 23), OC-1 and OC-2 are a primer pair capable of hybridizing to a beta-lactamase nucleic acid characteristic of the PSE1 (CARB-2, see page 19, right column), PSE4 (CARB-1, see page 19, right column) and CARB3 families of beta-lactamase enzymes wherein each primer of the pair includes 15-35 nucleotides as recited in (a) of the claim because these primers hybridize with CARB families of beta-lactamase during the process of amplifying CARB beta-lactamase gene probe. Since the results from colony hybridization assay show that No. 56 of E. Coli strain K12 has a known CARB-3 beta-lactamase gene and No. 58 of E. Coli strain K12 does not have a CARB-3 beta-lactamase

gene (see Table 1 in page 21), Nos. 56 and 58 of E. Coli strain K12 are positive and negative controls of CARB beta-lactamase respectively as recited in (b) of the claim. Since the method of Arlet *et al.,* includes amplification of beta-lactamase probes by PCR and identification of beta-lactamases in clinical strains by a hybridization assay, and are used to identify CARB beta-lactamases in clinical strains (see Table 1 in pages 20 and 21, right column in page 22, and left column in page 24), the method of Arlet *et al.,* is a protocol for identification of the beta-lactamase nucleic acid of characteristic of the PSE1, PSE4, or CARB3 family of beta-lactamase enzymes as recited in (c) of the claim.

Arlet *et al.,* do not disclose a bacteria diagnostic kit as recited in claim 56.

Fluit *et al.,* do teach a bacteria diagnostic kit (see pages 24 and 25).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have organized the components and method taught by Arlet *et al.,* into a kit because the method for identifying a beta-lactamase in a clinical sample using PCR is known at that time the inventions were made and the kit format is utilized not only to assemble a variety of different reagents together but ensure the quality and compatibility of the reagents. One having ordinary skill in the art at the time the invention was made would have been motivated to assemble reagent (s) of biotechnology methods into a kit in order to obtain the above discussed advantages, thus resulting in instant kit recited in claim 56. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to combine these prior art together because the kit would provide a convenient, efficient, economical way to practice the method of Arlet *et al.,*

***Response to Arguments***

In page 6, first paragraph of applicant's remarks, applicant argues that "[N]one of the cited art teaches or suggests the use of primers of 15-35 nucleotides pairs (as opposed to probes of much larger size as disclosed by Arlet) that are characteristic of the PSE1, PSE4, and CARB3 of beta-lactamase enzymes.".

This argument has been fully considered but it is not persuasive toward the withdrawal of the rejection because primers used by either Sandvang *et al.*, or Arlet *et al.*, are 20 bp (15-35 nucleotides) (see above rejection).

***Conclusion***

9. Claim 11 is allowed over prior art since SEQ ID NO: 32, SEQ ID NO: 33, and their fill-length complements are new.

10. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703)872-9306 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (571)272-0782.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

FRANK LU
PATENT EXAMINER

Frank Lu
PSA
April 26, 2004